the denervated than in the normal muscle. Staircase phenomenon is marked in the intact muscle and is usually absent or very slight in the denervated muscle.

The experiments permit the suggestion that these changes may be due to altered viscosity of the denervated muscle. J. F. Fulton[1] has proposed a similar explanation on the ground of the diminished tension and the increased area of the myograms showing the staircase effect.

Further investigation of these changes in muscle, on frogs and cats, is in progress. Preliminary observations on cats, in which the left sciatic was sectioned, indicate that the elasticity of the denervated muscle, as measured by the stretch produced by equal increments of load, is less than that of intact muscle subjected to the same experimental conditions.

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Production of a Premenstrual Endometrium in Castrated Monkeys by Ovarian Hormones.*

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The several theories explaining menstrual phenomena in primates for the most part agree that it depends upon hormonal function of the ovaries. Some authors emphasize follicular hormone, some corpus luteum, while others believe that both are concerned. Van Herwerden[1] found that in *Cercocebus cynomolgus* menstruation may occur without ovulation and Corner[2] and Allen[3] have established the same fact for *Macacus rhesus*. Allen also discovered that rather scanty menstruation in castrate and sexually immature monkeys usually followed after a certain degree of uterine growth had been induced by the injection of follicular hormone. These authors agree, however, that the uterine endometrium under these conditions is not typical of the normal premenstrual endometrium found only

[1] Fulton, J. F., "Muscular Contraction and the Reflex Control of Movement," 1926, 252.

* Assisted in part by a grant from the National Research Council, Committee on Problems of Sex.

[1] Van Herwerden, M., *Monatschr. f. Geburts u. Gynaek.*, 1906, xxiv, 730.

[2] Corner, G. W., *Contributions to Embryology*, 1923, No. 332, 75.

[3] Allen, E., *Contributions to Embryology*, 1927, xix, No. 380, 1.

when a corpus luteum is present. Novak[4] suggested that the physiology of menstruation could perhaps be solved if follicular and corpus luteum extracts of known potency were administered to experimental animals in the same sequence that they normally occur in the menstrual cycle.

Allen[3] has shown that physiologically active preparations of the follicular hormone do not promote typical premenstrual development of the uterine endometrium. We have made corpus luteum extracts which, in proper combination with follicular hormone, produce many physiological reactions ascribed to the normal corpus luteum (Hisaw,[5] Weichert,[6] Hisaw *et al*[7]). This paper reports the experimental use of these corpus luteum preparations on the production of premenstrual development of the uterine endometrium of castrate *Macacus rhesus* monkeys.

Five sexually mature female monkeys were castrated. They were first brought into full oestrum by the injection of follicular hormone (kindly furnished by E. R. Squibb & Sons) and then given a series

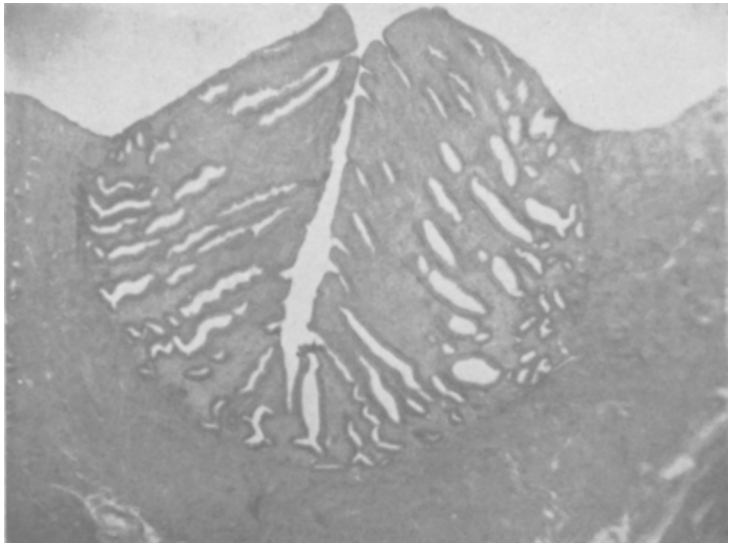

FIG. 1.

Monkey 4. Section through the lateral wall of the uterus of a castrate monkey which had received 340 units of follicular hormone followed by corpus luteum extract equivalent to 1040 gm. of fresh tissue.

[4] Novak, E., *J. Am. Med. Assn.*, 1928, xc, 339.

[5] Hisaw, F. L., *Physiol. Zool.*, 1929, ii, 59.

[6] Weichert, C. K., PROC. SOC. EXP. BIOL. AND MED., 1928, xxv, 490.

[7] Hisaw, F. L., Fevold, H. L., and Meyer, R. K., *Physiol. Zool.*, 1930, iii, 135.

of injections of corpus luteum extracts. Monkeys 4 and 5 received the largest dosage of corpus luteum extract and showed the best development of the uterine endometrium. These 2 animals received the following treatment:

Monkey 4 (Fig. 1). Experiment began 14 days after castration, received 340 rat units of follicular hormone during the next 10 succeeding days. This was followed immediately by the injection of corpus luteum extract for 7 days which totalled the equivalent of 1040 gm. of fresh corpus luteum tissue. The animal was sacrificed on the seventeenth day.

Monkey 5 (Fig. 2). Castrated 13 days after last menstruation. Right ovary contained a very large follicle while the left ovary had only small follicles and there were no corpora lutea in either ovary. This animal was used in the experiment immediately after castration and during the next 11 days received 305 rat units of follicular hormone. On the ninth, tenth, and eleventh days she was given 10, 10, and 5 rat units of follicular hormone in combination with a daily dose of corpus luteum extract equivalent to 260 gm. of fresh tissue. The corpus luteum treatment was continued for an additional 4 days, at the end of which time a total equivalent to 1690 gm. of fresh corpus luteum tissue had been used. The animal was sacrificed at the end of the sixteenth day.

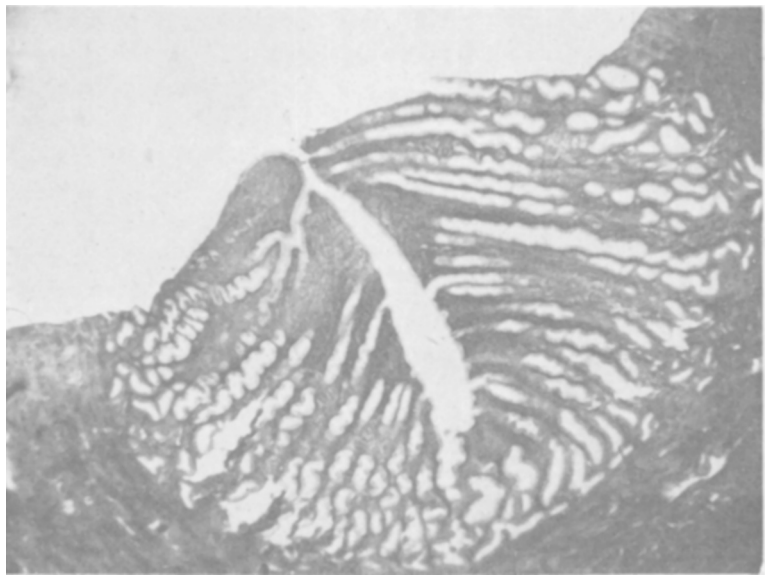

FIG. 2.

Monkey 5. Same as Fig. 1, except 305 rat units of follicular hormone and corpus luteum extract equivalent to 1690 gm. of fresh tissue were given.

We do not know whether or not the dosages used were excessive, but it should be mentioned that monkeys 1, 2 and 3 received corpus luteum extract equivalent to 360, 400 and 450 gm. respectively and while showing some modification of the endometrium were not nearly so favorable as animals 4 and 5, whose protocols are given. The accompanying figures do show, however, that it is possible to produce premenstrual changes in the uterus of castrate monkeys through the combined use of follicular and corpus luteum hormones.

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Physiology of Corpus Luteum VII. Maintenance of Pregnancy in Rabbit After Very Early Castration, by Corpus Luteum Extracts.

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In a recent series of papers[1] we have described the preparation and effects of an extract made from the *corpora lutea* of swine. When administered to recently spayed adult rabbits, or to immature rabbits whose uteri have been brought to the mature resting state by injections of oestrin, the *corpus luteum* hormone (progestin) induces alterations of the endometrium characteristic of pregnancy. If female rabbits are mated and castrated 18 hours later, while the fertilized ova are still in the Fallopian tube, the extracts substitute for the removed ovaries so completely that the embryos are nourished, become implanted, and develop in the uterus exactly as in normal pregnancy under the influence of the mother's own *corpora lutea*. In the third of our previous reports we have described 2 animals which were carried to the 13th and 19th days of pregnancy respectively. The demonstration of normal implantation with normal foetuses in these animals at autopsy led us to attempt to carry other animals through the full term, with the results now to be reported.

The procedure in general was as follows: A doe was mated, usually to 2 bucks, and was subjected to bilateral double oöphorectomy 18 hours after mating. The number of ruptured follicles in each ovary was noted. Administration of the extract by subcu-

[1] Corner, G. W., *Am. J. Physiol.*, 1928, lxxxvi, 74; Corner, G. W., and Allen, W. M., *Ibid.*, 1929, lxxxviii, 326; Allen, W. M., and Corner, G. W., *Ibid.*, 1929, lxxxviii, 340.